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(71) Applicant *(for all designated States except US)*: **CARDIAC PACEMAKERS, INC.** [US/US]; 4100 Hamline Avenue North, St. Paul, MN 55112-5798 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **GIROUARD, Steven, D.** [US/US]; 8155 Boulder Ridge Road, Woodbury, MN 55125 (US). **ROSS, Jeffrey** [US/US]; 3106 Fairview Avenue, Roseville, MN 55113 (US).

(74) Agents: **STEFFEY, Charles, E.** et al.; Schwegman, Lundberg, Woessner & Kluth, P.A., P.O. Box 2938, Minneapolis, MN 55402 (US).

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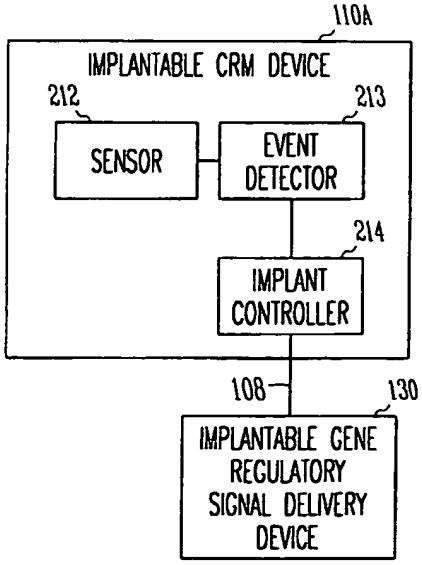
Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

[Continued on next page]

(54) Title: IMPLANTABLE SYSTEM FOR CONTROLLING GENE EXPRESSION



(57) Abstract: A gene regulatory system controls gene therapy by emitting one or more forms of energy that regulate gene expression by triggering promoters. The system includes a sensor to sense a signal indicative of a need for the gene therapy as well as responses to the gene therapy. The regulation of the gene expression is controlled based on the sensed signal and/or a user command. In one embodiment, the system delivers one or more electrical therapies in conjunction with the gene therapy.

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INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61N1/39 A61N1/362 A61M5/142 A61N1/32 A61K47/48
A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61N A61M A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2003/204206 A1 (PADUA RODOLFO A ET AL) 30 October 2003 (2003-10-30) abstract; figures 1,2,6,10-15 paragraph '0006! - paragraph '0014! paragraph '0053! - paragraph '0237!	1-3, 8-48,97
Y		4-51
X	US 2003/040777 A1 (SHEMER ITZIK ET AL) 27 February 2003 (2003-02-27) abstract; figure 1 paragraph '0012! - paragraph '0031! paragraph '0039!	1-3, 8-13,23, 32-34, 36,38, 39, 44-46,48

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 September 2005	20. 10. 2005
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Wetzig, T

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International Application No
PCT/US2005/006069

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2002/072785 A1 (NELSON CHESTER GARY ET AL) 13 June 2002 (2002-06-13) abstract; figure 5	49-51
P,X	WO 2004/080533 A (IMPULSE DYNAMICS NV; MIKA, YUVAL; SABBAH, HANI; HADDAD, WALID; ROUSSO,) 23 September 2004 (2004-09-23) the whole document	1-3, 8-48,97
Y	US 2002/049154 A1 (GRISSOM CHARLES B ET AL) 25 April 2002 (2002-04-25) abstract paragraphs '0008!, '0021!, '0038! - '0040!, '0086!, '0116! - '0121!	4-51
Y	WO 99/25385 A (IMARX PHARMACEUTICAL CORP) 27 May 1999 (1999-05-27) abstract page 2, line 22 - page 3, line 9 page 64, line 13 - line 25	5-51
X	WO 98/02150 A (MEDTRONIC, INC) 22 January 1998 (1998-01-22) abstract; figure 1 page 5, line 30 - page 7, line 32 page 8, line 24 - page 29, line 2	6
Y		7-51
Y	BUCHWALD A B ET AL: "Decoy oligodeoxynucleotide against activator protein-1 reduces neointimal proliferation after coronary angioplasty in hypercholesterolemic minipigs" JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY, vol. 39, no. 4, 20 February 2002 (2002-02-20), pages 732-738, XP002327401 ISSN: 0735-1097 the whole document	6-51
P,X	WO 2004/093969 A (MEDTRONIC, INC; LASKE, TIMOTHY, G; SIGG, DANIEL, C; SOYKAN, ORHAN) 4 November 2004 (2004-11-04) the whole document	6
Y	ZOU YUNZENG ET AL: "Heat shock transcription factor 1 protects cardiomyocytes from ischemia/reperfusion injury." CIRCULATION. 16 DEC 2003, vol. 108, no. 24, 16 December 2003 (2003-12-16), pages 3024-3030, XP002345863 ISSN: 1524-4539 the whole document	7-51

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2005/006069

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 52-96, 98-121
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [X] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[X] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-3, 8-51 (as far as dependent on claims 1-3), 97

   a device adapted to emit a gene regulatory signal on the basis of an electric field

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2. claims: 1, 4, 8-51 (as far as dependent on claim 4)

   a device adapted to emit a gene regulatory signal on the basis of optical energy

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3. claims: 1, 5, 8-51 (as far as dependent on claim 5)

   a device adapted to emit a gene regulatory signal on the basis of acoustic energy

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4. claims: 1, 6, 8-51 (as far as dependent on claim 6)

   a device adapted to emit a gene regulatory signal on the basis of a chemical agent

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5. claims: 1, 7, 8-51 (as far as dependent on claim 7)

   a device adapted to emit a gene regulatory signal on the basis of thermal energy

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US2005/006069

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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WO 2004093969 A	04-11-2004	NONE	